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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,005	07/18/2001	Henry Yue	PF-0599-2 DIV	9313

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/909,005	YUE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 29-46* is/are pending in the application.

4a) Of the above claim(s) *29,32,34,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,30,31,33,35-42 and 45-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. In view of the Appeal Brief filed on 5/9/03, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.
To avoid abandonment of the application, appellant must exercise one of the following two options:
(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,
(2) request reinstatement of the appeal.
If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

2. In view of the new grounds of rejection presented below, the present Office Action is made NON-FINAL.

Claims 10 and 29-46 are pending.

3. Claims 29, 32, 34 and 43-44 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 10, 30, 31, 33, 35-42 and 45-46 are under examination as as they read on an antibody which specifically binds to a polypeptide of SEQ IN NO: 1 and methods of making.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 35 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The term "specificity" recited in claims 35 and 38, line 1 is ambiguous and unclear and the metes and bounds of the claimed "specificity" is not defined.

7. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 10, 30, 31, 33, 35-42 and 45-46 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

Applicants are directed to the Revised Interim Utility Guidelines, Federal Register, Vol. 64, No.244, pages 71427-71440, Tuesday December 21, 1999. The final utility guidelines published in Jan. 2001and corresponding training materials (available on the PTO Website), none of the disclosed uses is a specific and/or substantial use.

9. The instant application has provided a description of antibodies to an isolated human CJPDZ polypeptide of SEQ ID NO:1 or a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1. The instant application does not disclose the biological role of the polypeptide or its significance. The instant specification asserts specific utilities for the claimed cell junction PDZ prptein, the polynucleotides encoding CJPDZ for the diagnosis, treatment or prevention of cancer, neurological disorders and developmental disorders, as well as disorders associated with increased CJPDZ expression or activity (on pages 3, lines 5-7 and 21, lines 9-11 in particular). The specification on page 4, lines 16-19, asserts that antagonists of the polypeptide of SEQ ID NO: 1 or fragments thereof can be used to teat or prevent a disorder associated with increased expression or activity of CJPDZ, wherein the antagonist can be antibody (page 6, lines 20-23). The specification also asserts that the claimed CJPDZ is involved in membrane-associated cell signaling (page 1, lines 17-21) and that the PDZ-containing proteins are likely involve in disorders associated with defective cell signaling, including developmental disorders, such as Williams syndrome, oncogenesis and neuronal function (page 2, lines 27-35). Further, the specification on page 29, discloses that the antibodies are useful for diagnostic purposes can be prepared and used for diagnostic assays for CJPDZ to detect CJPDZ in human body fluids or in extracts of cells or tissues.

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for CJPDZ polypeptide. The disclosed polypeptide is said to have a potential function based upon its amino acid sequence similarity to other known proteins such as LIN-7. The specification on page 12, discloses that CJPDZ and LIN-7 share 53% identity over all and 69% identity within the region from L25 to R204 of CJPDZ and from L117 to R295 of LIN-7. After further research, specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant specification has not identify even a single disease or disorder which has been shown to be associated with an "PDZ-containing proteins" of SEQ ID NO:1 or a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1 has not been shown to be differentially expressed in any disease or disorder, the claimed antibodies to the protein can not be employed in a diagnostic capacity. Further, the "PDZ-containing proteins" of SEQ ID NO: 1 has not been shown to be associated with a particular physiological process which an artisan would wish to manipulate for clinical effect by the administration of that protein or an agonist or antagonist thereof. Because an artisan does not know if an agonist-induced response by the claimed protein enhance or inhibit cell:cell communication. Walke *et al* in Curr Opin. Biotechnol. 2001, teach that a vast number of

genes of unknown function threaten to clog drug discovery pipelines. Further, Walke *et al* teach that in order to develop therapeutic products from novel genomic targets, it will be necessary to correlate biology with gene sequence information. Walke *et al* further teach that the validated drug target must be demonstrated in vivo to be a key switch in mammalian physiology with therapeutic applications (see abstract).

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this board interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the CJPDZ of the instant application was, as of the filling date, useful for EGF-mediated signaling, or deleted in patients with Williams syndrome as is in LIM kinas 1 as stated at pages 2 and 24 of the specification or to diagnose, treat or prevent disorders associated with expression of CJPDZ (see pages 21-22 and 30-31). Examples of such disorders include cancers such as adenocarcinoma, leukemia, lymphoma. melanoma, myeloma, sarcoma. teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroids and uterus', neurological disorders such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema. Epidural abscess. suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system Disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurotibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system, cerebral Palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies. Myasthenia gravis, periodic paralyis, mental disorders including mood, anxiety, and schizophrenic disorders, akathesia, amnesia, catatonia, diabetic neurophathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; and developmental disorders among other (see page 22 and 31). Until some actual and specific significance can be attributed to the protein identified in the specification as CJPDZ, one of

ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

No single effect of the disclosed CJPDZ of SEQ ID NO: 1 or a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1 is ascribed to the claimed protein and antibodies to the claimed protein. Note that while the specification produces the full-length protein recombinantly, no biological activity is established for the full length protein or any of the claimed a polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1. As such, further research would be required to identify or research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved would be required. Since the instant specification does not disclose a "real world" use for JCPDZ, then the claimed invention as disclosed does not meet the requirements of 35 U.S. C. § 101 as being useful.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 10, 30, 31, 33, 35-42 and 45-46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Further the specification does not reasonably provide enablement on how to make any antibody which specifically binds to any polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1 in claims 10 and 46 or a method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising: immunizing an antibody with "a polypeptide having an immunogenic fragment" of SEQ ID NO:1 in claims 35 and 38. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 12/02/02 and 6/20/02, respectively.

The instant claim language appears to encompass methods of making antibodies that binds to subsequences of SEQ ID NO:1. For example, claims 35 and 38 recite a polypeptide having an immunogenic fragment" of SEQ ID NO:1. Such a recitation does not require that the full length sequence set forth in SEQ ID NO:1; but rather encompasses any amino acid sequence

comprising either the full length of SEQ ID NO:1 or *any subsequence*. However, the specification does not appear to have provided sufficient guidance as to which subsequences of SEQ ID NO:1 would share the functional activity of SEQ ID NO:1. Neither does the specification appear to have provided any working examples of any functional subsequences. Thus it would require undue experimentation of the skilled artisan to determine which subsequences of SEQ ID NO:1would have the function of the full length molecule, and in turn make antibodies that bind these subsequences.

Applicants' arguments, filed 03/06/03, have been fully considered but not persuasive.

Applicants argue that the claim 10 recites not only that the variant polypeptides are at least 90% identical to SEQ ID NO:1, but also have "a naturally-occurring amino acid sequence." and the choice of amino acids to alter is made by nature. Contrary to Applicants' assertions, the specification fails to provide any naturally occurring amino acid sequence with 90% identity to SEQ ID NO:1 or defined the naturally occurring amino acid sequence at least 90% identical to the amino acid of SEQ ID NO:1. The specification on page 12, lines 10-18, provides only a 53 and overall 69% identity within the region from L25 to R204 of CJPDZ. Furthermore, CJPDZ contains a putative PDZ domain from R107 to T189 which shares 82% sequence identity with the PDZ domain of LIN-7. Furthermore, the specification on page 11, lines 16-23, defined a variant of CJPDZ polypeptide as an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes, ...More rarely, a variant may have "nonconservative" changes,... similar minor variations may also include amino acid deletions or insertions, or both.". The enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which 10% of the polypeptide would have been altered such that the resultant polypeptide would have retained the function of the starting polypeptide.

Applicant further asserts that one of skill in the art would be able to routinely obtain "a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1. Applicant provides example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the specification of the instant application. Applicant concluded that one skilled in the art need not make and test vast numbers of polypeptides that are based on the amino acid sequence of SEQ ID NO: 1. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature.

However, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to screen to identify the invention. Until the time when the at least 90% sequence identity polypeptides are found, then one skill in the art can make them.

Applicants argue that the Colman *et al*, Abaza *et al*, Lederman *et al* and Li *et al* references are not relevant to the case at hand. since the mutations were "artificially" created in the laboratory and therefore, are not analogous to molecular evolution, which is profoundly influenced by natural selection. Furthermore, amino acid residues that are critical for protein function are conserved. Thus, the amino acid differences are likely to represent substitutions that do not alter protein function. Contrary to Applicants' assertions. Lederman *et al*, teach a correlation between the genetic structure and the phenotype of the encoded protein in relation to the binding of mAbs, for example a common African allele of CD4, which is considered to be a naturally occurring event, has been identified by non-reactivity with the monoclonal antibody, OKT4. Lederman *et al*, further teaches that an arginin→ tryptophan substitution at amino acid 240 relative to $CD4^{OKT+}$ is found in chimpanzee, rhesus macaque, mouse and rat CD4 suggesting that this mutation may confer unique functional properties to the $CD4^{OKT4-}$ protein. Therefore, Lederman *et al* demonstrated that even a single amino acid change can ablate binding of the monoclonal antibody. Furthermore, Colman *et al* teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Colman *et al* provide an example of escape mutants of viral antigens which were selected by growth of virus in the presence of monoclonal antibody (natural selection), provide many examples of the type of substitution which can render the antigen unrecognizable by the selection antibody.

Applicants argue that Ngo *et al* reference cited by the Examiner relating to structure-antigenicity relationships in proteins is simply not germane to whether one can make and use the polypeptide variants recited by the present claims regardless of the function of the SEQ ID NO:1 variants , one can make those polypeptide variants using the disclosure. Applicants further bring to the Examiner's attention Brennet *et al* reference, wherein Brennet *et al* have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. Contrary to Applicant's assertions, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1 is essential for maintain its functional activity and which changes can be made in the structure of SEQ ID NO: 1 and still maintained the same function.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention with the different antibodies as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

12. Claims 10, 30, 31, 33, 35-42 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 12/02/02 and 6/20/02, respectively.

Applicants' arguments, filed 03/06/03, have been fully considered but not persuasive.

Applicant is in possession of an antibody which specifically binds to a polypeptide of SEQ ID NO:1; however, applicant is not in possession of any antibody which specifically binds to any polypeptide comprising any naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1 in claims 10 and 46 or a method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising: immunizing an antibody with "a polypeptide having an immunogenic fragment" of SEQ ID NO:1 in claims 35 and 38. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Applicants assert that the instant specification provides an adequate written description of the claimed antibodies which specifically bind to the recited "variants" of SEQ ID NO:1. Applicant noted that the "variant" language is limited to "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1." Applicant asserts that one of ordinary skill in the art would recognize polypeptide sequences which are variants having a polypeptide sequence at least 90% identical to SEQ ID NO: 1. Applicant concludes that the specification provides an adequate written description of the recited polypeptide variants of SEQ ID NO:1.

However, to satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563. The written-description requirement can be satisfied "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572. As for the recitation of "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1", the court has affirmed that all of the claims of a patent were invalid because the specification did not provide an adequate written description of the rat DNA that was required by the asserted claims. The court said that " an adequate written description of a DNA ... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.' Not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566 (quoting *Fiers*, 984 F.2d at 1171). Likewise, Applicant fails to satisfy the written-description requirement where the claimed invention called for a "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" and "a polypeptide having an immunogenic fragment", but did not disclose such "variants" and "fragments". The court stated that "an adequate written description of a DNA requires more than a mere statement that it is part

of the invention and reference to a potential method for isolating it, what is required is a description of the DNA itself." *Fiers* 984 F.2d at 1170.

Applicant argues that the present claims define the claimed genus through the recitation of chemical structure of a CJPDZ protein of SEQ ID NO:1 and that instant claims do not define a genus which is "highly variant". Applicant asserts that the situation in Lilly and *Fiers,* the claims at issue in the present application define the polypeptides bound by the claimed antibodies in terms of chemical structure, rather than functional characteristics.

Contrary to Applicant assertion the "naturally occurring" language in the claims is analogous to the claims found in *Lilly* and *Fiers* because the claimed polypeptides are defined only by their homology to SEQ ID NO:1, which is insufficient to satisfy 112(1) since "a mere wish or plan" for obtaining an invention is not enough to comply with 112(1). Furthermore, there is no described or art-recognized correlation or relationship between the structure of the invention, the CJPDZ protein and it's function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of fragments and variants, wherein the variant has at least 90% sequence identity of SEQ ID NO: 1.

Applicant asserts that the state of the art at the time of the present invention is further advanced than at the time of the Lilly and Fiers applications

Applicant contends that much has happened in the development of recombinant DNA technology in the 20 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. Appellant indicates that, for example, PCR, highly efficient cloning and DNA sequencing technology has been developed. Applicant asserts that with the current advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO: 1 and the additional extensive detail provided by the application, the present inventors were in possession of the claimed antibodies that bind specifically to 'variants' of SEQ ID NO: 1 at the time of filing of this application.

The broad brush discussion of making and screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the polypeptide CJPDZ of SEQ ID NO: 1 is disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent. No. 6,051,374 (of record) in view of U.S. Patent No. 6,210,675 (of record).

The '374 patent teaches a 5 amino acid immunogenic fragment of the claimed SEQ ID NO:1 (see sequence alignment in particular).

The claimed invention differs from the reference teachings only by the recitation of an antibody which specifically binds to an immunogenic fragment in claims 36 and 39; a composition comprising an antibody and an acceptable excipient in claims 37 and 40; a composition wherein the antibody is labeled in claim 33; a method of preparing a polyclonal antibody in claim 35; a method of making a monoclonal antibody in claim 38.

The '675 patent teaches that an antigenic fragment of an antigen having a minimum of five amino acids and each fragment is usually coupled to some carrier molecule to facilitate the induction of an immune response (column 2, lines 41-65 and column 3, lines 1-5 in particular). Furthermore, the '675 patent teaches antibodies and methods of producing polyclonal and monoclonal antibodies to a polypeptide (column 5, lines 5-47). Polyclonal antibodies against a polypeptide can be obtained by injecting a polypeptide, into a mammalian host such as a mouse, rat, sheep or rabbit and recovering the antibody thus produced; plasma samples being taken at appropriate intervals are assay for the antibody specificity. Monoclonal antibodies against a polypeptide can be obtained by fusing cells of an immortalizing cell line with cells which produce antibody against the polypeptide, and culturing the fused immortalized cell line. Also, the '675 patent teaches that antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection (column 5, lines 6-13 in particular). Finally, the '675 patent teaches that the antibody is in solution (column 7, lines 58-62 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the peptide taught by the '374 patent to make monoclonal and polyclonal antibodies as taught by '675 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antigenic fragment would facilitate the induction of an immune response to produce antibodies and the antibodies produced can be used in quality control testing of the polypeptide, purification of the polypeptide or lysate, epitope mapping and for antibody detection as taught by the '675 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 10, 36, 39, 41, 42 and 45-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset *et al* (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586).

Rousset *et al* (1997) teach a TAX interaction protein 33, a 202 amino acid polypeptide, which has 100% homology to claimed SEQ ID NO: 1 at positions (aa 32-233) (see sequence alignment in particular). Rousset et al (1997) further teach that the HTLV-1 Tax oncoprotein mediates interaction with the PDZ domain of cellular proteins. Further as evidenced by Rousset et al (1998) that the said polypeptide has high homology to the C. elegans LIN-7 protein. LIN-7 localizes LET-23 to cell junctions and human LIN-7 is likely to exhibit a similar function and to participate also in the clustering of transmembrane receptors (see page 650, 2nd column 1st paragraph in particular).

The claimed invention differs from the reference teachings only by the recitation of an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO:1 in claims 10(a) and 45, a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 in claims 10(b) claim 46.

Campbell teaches that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (see page 3 figure 11.1 in particular). One field of research in which monoclonal antibodies may prove of particular value is in the study of chromosomal proteins. The search for those chromosomal proteins which are responsible for determining cell phenotype has been particularly long and comparatively fruitless and monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins. As hybridoma production becomes a more routine laboratory technique (see page 29 and 30 under Basic research in particular).

As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, which mean that "specifically bind" with both proteins. Bost et al (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

Claims 36, 39, 41 and 42 are included because an antibody is the same antibody irrespective of how it is made.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to to make a monoclonal antibody as taught by Campbell against the 202 amino acid polypeptide taught by the Rousset et al (1997).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it was customary at the time the invention was made to make monoclonals against any new macromolecule as taught by Campbell for the search for those chromosomal proteins which are responsible for determining cell phenotype and because the monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Claims 10, 36, 39, 41, 42 and 45-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586).

Rousset *et al* (1998) teach a TAX interaction protein 33, a 202 amino acid polypeptide, which has 100% homology to claimed SEQ ID NO: 1 at positions (aa 32-233) (see sequence alignment in particular). Rousset et al (1998) further teach that the HTLV-1 Tax oncoprotein mediates interaction with the PDZ domain of cellular proteins. Rousset *et al* (1998) teach that the said polypeptide has high homology to the C. elegans LIN-7 protein. LIN-7 localizes LET-23 to cell junctions and human LIN-7 is likely to exhibit a similar function and to participate also in the clustering of transmembrane receptors (see page 650, 2nd column 1st paragraph in particular).

The claimed invention differs from the reference teachings only by the recitation of an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO:1 in claims 10(a) and 45, a polypeptide comprising a naturally occurring amino acid

sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 in claims 10(b) claim 46.

Campbell teaches that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (see page 3 figure 11.1 in particular). One field of research in which monoclonal antibodies may prove of particular value is in the study of chromosomal proteins. The search for those chromosomal proteins which are responsible for determining cell phenotype has been particularly long and comparatively fruitless and monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins. As hybridoma production becomes a more routine laboratory technique (see page 29 and 30 under Basic research in particular).

As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, which mean that "specifically bind" with both proteins. Bost *et al* (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

Claims 36, 39, 41 and 42 are included because an antibody is the same antibody irrespective of how it is made.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to to make a monoclonal antibody as taught by Campbell against the 202 amino acid polypeptide taught by the Rousset et al (1998).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it was customary at the time the invention was made to make monoclonals against any new macromolecule as taught by Campbell for the search for those chromosomal proteins which are responsible for determining cell phenotype and because the monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. Claims 35-36 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset *et al* (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost

et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Harlow (1989).

The teachings of the Rousset *et al* references, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a polyclonal antibody in claim 35 and monoclonal antibody in claim 38.

Harlow *et al* teach a method of producing polyclonal antibody to any antigen (see entire document and page 96, in particular). Harlow *et al* further teach that for practical reasons, rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Further, Harlow et al teach a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. fragments), harvesting spleen cells from said animal, fusing said spleen cells with myeloma cell line, and culturing said fused cells (i.e hybridoma) under conditions that allow production of said antibody. Harlow et al further teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities (see pages 141-157 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody using the method taught by Harlow *et al* with the polypeptide of Tax interacting protein 33 taught by Rousset *et al.*

One ordinary skill in the art at the time the invention was made would have been motivated to make polyclonal antibody to Tax interacting protein 33 because Harlow *et al* teach rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Harlow *et al* further the monoclonal antibodies produced exhibit a high degree of specificity and great affinity.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Claims 35-36 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Harlow (1989).

The teachings of the Rousset *et al*, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a polyclonal antibody in claim 35 and monoclonal antibody in claim 38.

Harlow *et al* teach a method of producing polyclonal antibody to any antigen (see entire document and page 96, in particular). Harlow *et al* further teach that for practical reasons, rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Further, Harlow et al teach a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. fragments), harvesting spleen cells from said animal, fusing said spleen cells with myeloma cell line, and culturing said fused cells (i.e hybridoma) under conditions that allow production of said antibody. Harlow et al further teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities (see pages 141-157 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody using the method taught by Harlow *et al* with the polypeptide of Tax interacting protein 33 taught by Rousset *et al.*

One ordinary skill in the art at the time the invention was made would have been motivated to make polyclonal antibody to Tax interacting protein 33 because Harlow *et al* teach rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Harlow *et al* further the monoclonal antibodies produced exhibit a high degree of specificity and great affinity.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset *et al* (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Owens *et al* (1994) (of record).

The teachings of the Rousset *et al* references, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody.

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody antibodies monoclonal antibody technology, chimeric, single chain, Fab fragments, and $F(ab')_2$. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement – dependent cytotoxcity (see the entire document).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make a monoclonal/polyclonal antibody as taught by Campbell or Harlow against the Tax interacting portein 33 taught by the Rousset *et al* and produce the antibody as chimeric, humanized antibody, Fab and $F(ab')_2$ fragments taught by the Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al*. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Owens *et al* (1994) (of record).

The teachings of the Rousset *et al*, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody.

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody antibodies monoclonal antibody technology, chimeric, single chain, Fab fragments, and $F(ab')_2$. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the

human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement – dependent cytotoxcity (see the entire document).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make a monoclonal/polyclonal antibody as taught by Campbell or Harlow against the Tax interacting portein 33 taught by the Rousset *et al* and produce the antibody as chimeric, humanized antibody, Fab and F(ab')$_2$ fragments taught by the Owens *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

21. Claim 31, 33, 37, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset *et al* (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of U.S. Patent No. 6,210,675.

The teachings of Rousset *et al* references, Campbell reference, Bost *et al*, and the '675 patent have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a composition comprising an antibody and an acceptable excipient in claims 31, 37 and 40 and a composition wherein the antibody is labeled in claim 33.

The '675 patent teaches that an antigenic fragment of an antigen having a minimum of five amino acids and each fragment is usually coupled to some carrier molecule to facilitate the induction of an immune response (column 2, lines 41-65 and column 3, lines 1-5 in particular). Furthermore, the '675 patent teaches antibodies and methods of producing polyclonal and monoclonal antibodies to a polypeptide (column 5, lines 5-47). Polyclonal antibodies against a polypeptide can be obtained by injecting a polypeptide, into a mammalian host such as a mouse,

rat, sheep or rabbit and recovering the antibody thus produced; plasma samples being taken at appropriate intervals are assay for the antibody specificity. Monoclonal antibodies against a polypeptide can be obtained by fusing cells of an immortalizing cell line with cells which produce antibody against the polypeptide, and culturing the fused immortalized cell line. Also, the '675 patent teaches that antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection (column 5, lines 6-13 in particular). Finally, the '675 patent teaches that the antibody is in solution (column 7, lines 58-62 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to formulate the antibody in a composition and to link the antibody to a label as taught by `675 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the composition antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection as taught by '675 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

22. Claims 31, 33, 37, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset *et al* (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of U.S. Patent No. 6,210,675.

The teachings of Rousset *et al*, Campbell reference, Bost *et al*, and the `675 patent have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a composition comprising an antibody and an acceptable excipient in claims 31, 37 and 40 and a composition wherein the antibody is labeled in claim 33.

The '675 patent teaches that an antigenic fragment of an antigen having a minimum of five amino acids and each fragment is usually coupled to some carrier molecule to facilitate the induction of an immune response (column 2, lines 41-65 and column 3, lines 1-5 in particular). Furthermore, the '675 patent teaches antibodies and methods of producing polyclonal and monoclonal antibodies to a polypeptide (column 5, lines 5-47). Polyclonal antibodies against a polypeptide can be obtained by injecting a polypeptide, into a mammalian host such as a mouse,

rat, sheep or rabbit and recovering the antibody thus produced; plasma samples being taken at appropriate intervals are assay for the antibody specificity. Monoclonal antibodies against a polypeptide can be obtained by fusing cells of an immortalizing cell line with cells which produce antibody against the polypeptide, and culturing the fused immortalized cell line. Also, the '675 patent teaches that antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection (column 5, lines 6-13 in particular). Finally, the '675 patent teaches that the antibody is in solution (column 7, lines 58-62 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to formulate the antibody in a composition and to link the antibody to a label as taught by '675 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the composition antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection as taught by '675 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor. Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

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